

### **REMARKS**

Upon entry of the present amendment, claims 26, 41-45, and 48-50 are pending in the application. The amendment to claim 26 and new claims 48-50 are supported by disclosure at page 5, lines 1-19, of the specification.

No new matter has been added.

#### **I. Rejections under 35 U.S.C. § 103**

Claims 26, 42, 46, and 47 were rejected for obviousness over Lavaissiere et al. as evidenced by Kelley et al. and Leck-Czernik et al. in view of Jia et al. In the paragraph spanning pages 4-5 of Paper No. 14, the Examiner stated:

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to administer to the liver of a mammal having hepatocellular carcinoma, a mutant of the HAAH polypeptide, wherein said mutation comprises a substitution of alanine for histidine at residue 675. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Lavaissiere et al. correlating the increase in hydroxylation of NOTCH to the increase in the activity of the cytoplasmic domain of NOTCH which is known to be oncogenic, and the further teachings of Lavaissiere et al. identifying histidine in the His motif of HAAH which is necessary for the hydroxylation activity of HAAH and the teaching that said His motif is identical to the His motif found in bovine , aspartyl (asperaginyl) hydroxylase; and the teachings of Jia et al. demonstrating that mutation of the histidine at position 675 in bovine aspartyl (asperaginyl)hydroxylase results in the loss of hydroxylation activity of the enzyme. One of skill in the art would be motivated to decrease the hydroxylation of NOTCH in order to decrease the oncogenic activity of the cytoplasmic domain of NOTCH, and one of skill in the art would recognized that mutant HAAH polypeptide incapable of hydroxylating NOTCH would antagonize the hydroxylation activity of the wild-type HAAH polypeptide. (emphasis added)

The claims have now been amended to require that the compound be a HAAH mutant that contains a mutation at position 671, 679, or 690 of SEQ ID NO:2. The teachings of the prior art fail to describe or suggest the specific mutants now required by the amended claims. In view of this amendment, Applicants request withdrawal of this rejection.

#### **I. Rejections under 35 U.S.C. § 112**

Claim 46 and 47 were rejected under 35 U.S.C. § 112, second paragraph, and 35 U.S.C. § 112, first paragraph, respectively. The rejected claims have been canceled. Therefore, this rejection is moot.

### CONCLUSION

Applicants submit that the application is in condition for allowance and such action is respectfully requested.

A petition for extension of time and a check in the amount of \$420.00 is enclosed to cover the petition fee for a two-month extension of time pursuant to 37 C.F.R. § 1.17(a)(3). The Commissioner is hereby authorized to charge any fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0311, Reference No. 21486-032DIV4.

Should any questions or issues arise concerning the application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,



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Dated:

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